plotted as a function of the distance along the microchannel of FIG. **3**(*a*), and FIG. **3**(*d*) is a plot depicting velocity as a function of distance along the microchannel;

FIG. **4**(*a*) is a schematic illustration of a microchannel for temperature gradient focusing created by Joule heating according to another embodiment of the present invention, FIG. **4**(*b*) depicts the temperature profile along a length of the microchannel of FIG. **4**(*a*), FIG. **4**(*c*) depicts the electric field profile along a length of the microchannel of FIG. **4**(*a*), and FIG. **4**(*d*) is a plot showing electrophoretic velocity, bulk velocity, and total velocity vs. distance along the microchannel of FIG. **4**(*a*);

FIG. **5** is a schematic drawing of a fluidic device according to further embodiment of the present invention; and

FIG. **6** is a schematic drawing of a capillary fluidic device according to an alternate embodiment of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides temperature gradient focusing of a sample in a fluidic device which includes a fluid conduit such as a channel or capillary tube. Temperature gradient focusing focuses analytes by balancing the electrophoretic velocity of an analyte against the bulk velocity of the buffer containing the analyte. If there is an appropriate gradient in the electric field, the total velocity of a given charged analyte, as determined by the sum of the bulk and electrophoretic velocities, can be set to zero at any point along the channel and all the analyte in the system is moved toward that point. However, in contrast to electric field gradient focusing where the electric field gradient is applied using a combination of electrodes and membranes, using temperature gradient focusing of the present invention, the necessary electric field gradient is produced by the application of a temperature gradient.

Further description of the present invention will now be made with reference to the drawings, and in particular to FIG. **3**(*a*), where a buffer-filled microchannel **10** includes electrode connections **12**, **14** at each end. The velocity of an analyte in the microchannel **10** is given by the sum of its electrophoretic velocity, u_{EP}, and the bulk velocity, u_B, of the buffer:

$$u_T = u_{EP} + u_B.$$

If there is a gradient in the electrophoretic velocity, the bulk velocity can be adjusted so that the total velocity is equal to zero at a single point along the channel, and the analyte will be focused at that point. The electrophoretic velocity of an analyte in the microchannel **10** is given by the product of the electric field, E, and the electrophoretic mobility of the analyte: $u_{EP} = E \cdot \mu_{EP}$.

A temperature gradient is applied along the length of the channel as shown in FIG. **3**(*b*). This results in corresponding gradients in both the electric field E and the electrophoretic mobility μ_{EP}.

The electric field in the microchannel **10** is given by:

$$E = \frac{I}{A \cdot \sigma},$$

where I is the electric current running through the microchannel **10**, A is the channel cross-sectional area of the microchannel **10**, and σ is the conductivity of the buffer. Since the conductivity of the buffer is temperature-dependent, the electric field is also temperature-dependent. Here, constant current is presumed because the current running through any given section of the microchannel **10** will be the same for all parts of the microchannel, whereas the voltage drop across a portion of the microchannel **10** and the electric field in the microchannel **10** will depend on the temperature of that portion. One skilled in the art will readily appreciate that the present temperature gradient focusing differs from electric field gradient focusing in that in electric field gradient focusing, the velocity gradient that is used for focusing results from a gradient in the electric field imposed by the addition or subtraction or current from point or points within the microchannel.

Using microchannel **10**, it is possible to manipulate the conductivity of the buffer by changing the temperature. Consequently, it is possible to produce electric field gradients in microfluidic devices, such as microchannel **10**, through the application of a temperature gradient.

At fixed current density, the electric field in microchannel **10** is inversely proportional to the conductivity of the buffer solution in the microchannel. Most often, the primary temperature dependence of the conductivity is due to the variation of the solvent viscosity with temperature, so it can be written as $\sigma = \sigma_0 \cdot \eta(20)/(\eta(T) \cdot f(T))$, where σ is the conductivity, σ_0 is a constant, η(T) is the temperature dependent viscosity, and $f(T)$ is a function that accounts for any other temperature dependence. Similarly, the temperature dependence of the electric field is given by $E = E_0 \cdot \eta(T) \cdot f(T)/\eta(20)$, where E is the electric field and E_0 is a constant.

For most buffers, the function $f(T)$ is constant or only weakly dependent on temperature. However, it can be non-constant, i.e., variable, if, for example, the ionic strength of the buffer is temperature dependent. Advantageously, the buffers of the present invention are characterized by a non-constant $f(T)$.

The electrophoretic mobility of an ionic (e.g., analyte) species in the buffer is also dependent on the viscosity, and so can be written as $\mu_{EP} = \mu_0 \cdot \eta(20)/(\eta(T) \cdot f_{EP}(T))$, where μ_0 and $f_{EP}(T)$ are defined in analogy to σ_0 and $f(T)$ where, for most analytes, $f_{EP}(T)$ will be constant. The electrophoretic velocity of the analyte can then be written as $u_{EP} = E_0 \cdot \mu_0 \cdot f(T)/f_{EP}(T)$. It should be noted that if $f(T)$ and $f_{EP}(T)$ have the same temperature dependence, e.g., they are both constant, then u_{EP} will not be temperature dependent, and an electric field gradient produced in this way can not be used for focusing.

If, on the other hand, $f(T)$ and $f_{EP}(T)$ do not have the same temperature dependence, then temperature gradients will result in gradients in the electrophoretic velocity, which can be used for focusing as described above.

One skilled in the art will readily appreciate a major advantage of this present method over some other methods of preconcentration is that the concentration of the buffer salts is completely unaffected by the focusing. This results from the fact that if the buffer salt is considered as an analyte, then, by definition, $f_{EP}(T) = f(T)$ and there is no gradient in the electrophoretic velocities of the buffer salts.

Most commonly this technique would be implemented with a buffer characterized by a strongly temperature dependent $f(T)$ and with analytes characterized by a constant or nearly constant $f_{EP}(T)$. However, the present temperature gradient focusing can also be implemented in a system in which $f(T)$ is constant and $f_{EP}(T)$ is not, or in which both $f(T)$ and $f_{EP}(T)$ are non-constant, but differ in their temperature dependence.